

SUPPLEMENTARY MATERIAL

Table S1: Clinical presentation and analytical results according to smoking status.

SYMPTOMS n (%)	Smoker N=307	Ex-smoker N=934	Non-smoker N=3983	p value
Asymptomatic	35 (11.4) † *	35 (3.8)	189 (4.8)	p<0.001
Mild dyspnoea	66 (21.5)	243 (26.0)	1078 (27.1) ¥	
Moderate dyspnoea	54 (17.6)	207 (22.2)	794 (19.9)	
Severe dyspnoea	29 (9.4)	123 (13.2) *	346 (8.7)	
Tachypnoea	73 (24.3)	301 (33.7) * ¥	1004 (26.1)	p<0.001
Fatigue	126 (42.1)	444 (49.6) ¥	1797 (46.4)	p=0.059
Anosmia	49 (16.7) † *	47 (5.5)	261 (7.0)	p<0.001
Disgeusia	53 (18.0) † *	50 (5.8)	280 (7.5)	p<0.001
Sore throat	46 (15.6) †	79 (9.1)	471 (12.5) †	p=0.003
Fever	222 (73.0)	722 (78.6) ¥	3164 (80.3) ¥	p=0.007
Cough	200 (65.6)	623 (68.2)	2664 (67.8)	p=0.681
Vomiting	18 (6.0)	55 (6.1)	312 (8.1) †	p=0.074
Diarrhea	56 (18.7)	171 (19.1)	751 (19.5)	p=0.920
Myalgia	87 (28.8)	265 (29.7)	1288 (33.5) †	p=0.035
Oxygen saturation<92%	96 (31.9)	408 (45.0) * ¥	1309 (34.0)	p<0.001
ANALYTICAL RESULTS				
Elevated Ddimer	155 (57.4)	583 (72.4) * ¥	2129 (62.9)	p<0.001
Elevated procalcitonin	58 (24.7)	187 (28.4) *	567 (19.7)	p<0.001
Elevated CRP	253 (85.8)	839 (93.0) * ¥	3406 (88.4)	p<0.001
Elevated troponin	52 (27.8) † *	73 (17.2) *	255 (12.4)	p<0.001
Elevated transaminases	106 (37.7)	350 (41.3)	1463 (40.2)	p=0.573
Elevated ferritine	89 (47.3)	315 (62.6) ¥	1276 (59.3) ¥	p=0.001
Elevated triglycerides	52 (29.5)	80 (19.5) ¥	361 (19.8) ¥	p=0.008
Elevated LDH	153 (55.6) † *	630 (75.8)	2520 (71.8) †	p<0.001
Creatinine >1,5	82 (27.6)	188 (20.8) ¥	479 (12.5) † ¥	p<0.001
Lymphocytes <1500	160 (54.6) † *	728 (82.4)	2972 (77.9) †	p<0.001
Hemoglobin<12 gr/dl	97 (32.3)	241 (26.8)	991 (25.7) ¥	p=0.040
Platelets<150000	81 (27.1)	271 (30.0)	918 (23.8) †	p<0.001
<i>LDH; lactate dehydrogenase. CRP; C reactive protein. HB; hemoglobin. CR; creatinine. TN; troponin. Values are n (%). All p values were determined by using an analysis of variance with Bonferroni method. * p < 0.05 compared to non-smoker subjects. † p < 0.05 compared to ex-smokers. ¥ p<0.05 compared to smoker subjects.</i>				

Table S2: Treatment during in-hospital stay.

IN-HOSPITAL MANAGEMENT				
OXYGEN THERAPY n (%)	Smoker	Ex-Smoker	Non-smoker	p value
O ₂ at the admission	186 (61.0)	740 (81.3) * ¥	2744 (69.8) ¥	p<0.001
High flow nasal cannula	72 (23.8) *	199 (22.1) *	723 (18.7)	p=0.013
Non-invasive mechanical ventilation	43 (14.1)	159 (17.5) *	486 (12.5)	p<0.001
Invasive mechanical ventilation	26 (8.6)	91 (10.1) *	277 (7.2)	p=0.009
Prone position	22 (7.4)	136 (15.1) * ¥	374 (9.7)	p<0.001
Circulatory support or ECMO	13 (4.3)	61 (6.8) *	167 (4.3)	p=0.007
OTHER THERAPIES DURING THE ADMISSION, n (%)				
Use of glucocorticoids	75 (25.2)	328 (36.4) * ¥	1028 (26.5)	p<0.001
Use of hydroxychloroquine	256 (85.0)	794 (87.2) *	3296 (83.8)	p=0.04
Use of antiviral drugs	189 (62.6)	566 (62.2)	2299 (58.7)	p=0.08
Use of interferon	80 (26.8) † *	144 (16.1) *	451 (11.7)	p<0.001
Use of tocilizumab	26 (8.7)	93 (10.4) *	317 (8.2)	p=0.097
Use of antibiotics	210 (72.7)	704 (81.3) * ¥	2831 (75.8)	p=0.001
Use of ACEI /ARBs	75 (25.0) *	232 (26.3) *	644 (17.0)	p<0.001
Use of anticoagulants				p<0.001
PROFILACTIC	91 (48.1)	319 (58.6) ¥	1273 (55.2)	
<i>ECMO; extracorporeal membrane oxygenation. ACEI; Angiotensin-converting enzyme inhibitors. ARBs; Angiotensin II receptor blockers.</i>				
<i>Values are n (%). All p values were determined by using an analysis of variance with Bonferroni method. * p < 0.05 compared to non-smoker subjects. † p < 0.05 compared to ex-smokers. ¥ p < 0.05 compared to smoker subjects.</i>				

Table S3: Complications during in-hospital stay, including ICU admission and Prone position according to age.

COMPLICATIONS n (%)		SMOKING STATUS			p value
		Smoker N=307	Former smoker N=934	Non-smoker N=3983	
Hypotension		25 (8.5)	81 (9.6) *	262 (7.2)	p=0.057
Respiratory insufficiency		140 (46.1)	576 (62.8) * ¥	1908 (48.5)	p<0.001
Heart failure		19 (6.3)	104 (11.5) * ¥	213 (5.4)	p<0.001
Renal failure		57 (18.9) *	222 (24.4) * ¥	559 (14.3)	p<0.001
URTI		31 (10.3)	130 (14.6) *	467 (12.1)	p=0.069
Sepsis		71 (23.6) † *	132 (14.6) *	375 (9.6)	p<0.001
SIRS		48 (15.9)	235 (26.2) * ¥	743 (19.1)	p<0.001
Bilateral pneumonia		158 (51.5)	702 (75.2) * ¥	2804 (70.4) ¥	p<0.001
Unilateral pneumonia		70 (22.8) † *	126 (13.5)	635 (15.9)	
Relevant bleeding		12 (4.0)	34 (3.8) *	92 (2.4)	p=0.024
Hemoptysis		14 (4.6) *	24 (2.7) *	53 (1.4)	p<0.001
Embolic events		13 (4.3) *	30 (3.3) *	66 (1.7)	p<0.001
Skin rash		22 (10.0) † *	16 (2.6)	61 (2.2)	p<0.001
ICU ADMISSION		30 (9.9)	82 (8.9)	230 (5.9)	p<0.001
Age	<52	7 (8.0)	6 (6.7)	60 (5.2)	p=0.45
	52-66	18 (15.8)	23 (9.9)	86 (8.9)	p=0.06
	66-77	3 (4.5)	41 (11.8)	73 (8.5)	p=0.07
	>77	2 (5.4)	12 (4.8)	11 (1.2)	p=0.001
PRONE POSITION		22 (7.4)	134 (15.2)	368 (9.7)	p<0.001
Age	<52	7 (8)	8 (9.3)	89 (7.9)	p=0.89
	52-66	6 (5.4)	28 (12.6)	119 (12.7)	p=0.07
	66-77	6 (9.1)	71 (21.2)	112 (13.4)	p=0.001
	>77	3 (9.1)	27 (11.2)	48 (5.3)	p=0.04

*SIRS: systemic inflammatory response syndrome; URTI: upper respiratory tract infection. Hypotension: systolic pressure <90 mmHg. Values are n (%). P values were determined by using an analysis of variance with Bonferroni method. * p < 0.05 compared to non-smoker subjects. † p < 0.05 compared to ex-smokers. ¥ p<0.05 compared to smoker subjects.*

Table S4: All-cause in-hospital death according to three different smoking patterns, stratified by age.

ALL-CAUSE DEATH n (%)	Smoking status			P value
	Current smoker N=307	Ex-smoker N=934	Non-smoker N=3983	
n=1336 <52	4 (4.6%)	9 (10%)	52 (4.5%)	p=0.06
n=1312 52-66	13 (11.4%)	28 (12.1%)	92 (9.5%)	p=0.46
n=1276 66-77	25 (37.9%)	109 (31.4%)	161 (18.7%)	p<0.001
n=1217 >77	19 (51.4%)	129 (52%)	418 (44.8%)	p=0.11
All patients (n=5141)	61 (20.1%)	275 (30%)	723 (18.4%)	p<0.001

Table S5. All-cause in-hospital mortality and the combined endpoint (ICU admission, prone, death).

IN-HOSPITAL OUTCOMES n (%)	Current smoker and former smoker n=1241	Non-smoker n=3983	p value
ALL-CAUSE DEATH /5224	343 (27.6)	734 (18.4)	p<0.001
ICU ADMISSION	114 (9.2)	234 (5.9)	p<0.001
PRONE POSITION	158 (13.2)	374 (9.7)	p=0.001
COMBINED ENDPOINT/5100 (Death, prone, ICU admission)	439 (36.2)	1013 (26.1)	p<0.001

Table S6: Propensity scores for mortality and the combined endpoint. Smokers (current or former) vs. never smokers.

Propensity score			
	OR	95% CI	p
All-cause death	1.04	0.99-1.07	p=0.06
Combined endpoint*	1.05	1.00-1.10	p=0.03
<i>*all-cause death, prone position, ICU admission.</i>			